Author Correction: Lineage tracing of acute myeloid leukemia reveals the impact of hypomethylating agents on chemoresistance selection

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Abstract: An amendment to this paper has been published and can be accessed via a link at the top of the pape Chemotherapy-resistant cancer recurrence is a major cause of mortality. In acute myeloid leukemia (AML), chemorefractory relapses result from the complex interplay between altered genetic, epigenetic and transcriptional states in leukemic cells. Here, we develop an experimental model system using in vitro lineage tracing coupled with exome, transcriptome and in vivo functional readouts to assess the AML population dynamics and associated molecular determinants underpinning chemoresistance development. We find that combining standard chemotherapeutic regimens with low doses of DNA methyltransferase inhibitors (DNMTi, hypomethylating drugs) prevents chemoresistant relapses. Mechanistically, DNMTi suppresses the outgrowth of a pre-determined set of chemoresistant AML clones with stemness properties, instead favoring the expansion of rarer and unfit chemosensitive clones. Importantly, we confirm the capacity of DNMTi combination to suppress stemness-dependent chemoresistance development in xenotransplantation models and primary AML patient samples. Together, these results support the potential of DNMTi combination treatment to circumvent the development of chemorefractory AML relapses.

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